Claims

1. A method of diagnosing a disorder characterized by expression of a cancer associated antigen precursor coded for by a nucleic acid molecule, comprising:

contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with a MHC molecule, wherein the nucleic acid molecule is a NA Group 1 molecule, and

determining the interaction between the agent and the nucleic acid molecule or the expression product as a determination of the disorder.

2. The method of claim 1, wherein the agent is selected from the group consisting of

(a) a nucleic acid molecule comprising NA group 1 molecules or a fragment thereof,

(b) a nucleic acid molecule comprising NA group 3 molecules or a fragment thereof,

(c) a nucleic acid molecule comprising NA group 5 molecules or a fragment thereof,

(d) an antibody that binds to an expression product of NA group 1 molecules,

(e) an antibody that binds to an expression product of NA group 3 molecules,

(f) an antibody that binds to an expression product of NA group 5 molecules,

(g) an agent that binds to a complex of a MHC molecule and a fragment of an expression product of a NA group 1 molecule,

(h) an agent that binds to a complex of a MHC molecule and a fragment of an expression product of a NA group 3 molecule, and

(i) an agent that binds to a complex of a MHC molecule and a fragment of an expression product of a NA group 5 molecule.

3. The method of claim 1, wherein the disorder is characterized by expression of a plurality of cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8, at least 9 or at least 10 such agents.

4. The method of claims 1-3, wherein the agent is specific for a cancer associated antigen precursor that is a fibrosarcoma cancer associated antigen precursor.

5. The method of claim 2, wherein the NA group 1 molecule is SEQ ID NO:23.

6. A method for determining regression, progression or onset of a condition characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising

monitoring a sample, from a patient who has or is suspected of having the condition, for a parameter selected from the group consisting of

(i) the protein,

(ii) a peptide derived from the protein,

(iii) an antibody which selectively binds the protein or peptide, and

(iv) cytolytic T cells specific for a complex of the peptide derived from the protein and an MHC molecule,

as a determination of regression, progression or onset of said condition.

7. The method of claim 6, wherein the sample is a body fluid, a body effusion or a tissue.

8. The method of claim 6, wherein the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of

(a) an antibody which selectively binds the protein of (i), or the peptide of (ii),

(b) a protein or peptide which binds the antibody of (iii), and

(c) a cell which presents the complex of the peptide and MHC molecule of (iv).

9. The method of claim 8, wherein the antibody, the protein, the peptide or the cell is labeled with a radioactive label or an enzyme.

10. The method of claim 6, comprising assaying the sample for the peptide.

11. The method of claim 6, wherein the nucleic acid molecule is a NA Group 3 molecule.

12. The method of claim 6, wherein the nucleic acid molecule is a NA Group 5 molecule.

13. The method of claim 6, wherein the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins, at least one of which is a cancer associated protein encoded by a NA Group 1 molecule.

14. The method of claim 6, wherein the NA Group 1 molecule is SEQ ID NO:23.

15. A pharmaceutical preparation comprising

an agent which when administered to the subject enriches selectively the presence of complexes of a MHC molecule and a cancer associated antigen, and

a pharmaceutically acceptable carrier, wherein the cancer associated antigen is a fragment of a cancer associated antigen precursor encoded by a nucleic acid molecule comprising a NA Group 1 molecule.

16. The pharmaceutical preparation of claim 15, wherein the agent comprises a plurality of agents, each of which enriches selectively in the subject complexes of a MHC molecule and a different cancer associated antigen, wherein at least one of the cancer associated antigens is encoded by a NA Group 1 molecule.

17. The pharmaceutical preparation of claim 16, wherein the plurality is at least two, at least three, at least four or at least 5 different such agents.

18. The pharmaceutical preparation of claim 15, wherein the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

19. The pharmaceutical preparation of claim 15, wherein the agent is selected from the group consisting of

(1) an isolated polypeptide comprising the cancer associated antigen, or a functional variant thereof,

(2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, or functional variant thereof,

(3) a host cell expressing the isolated polypeptide, or functional variant thereof, and

(4) isolated complexes of the polypeptide, or functional variant thereof, and a MHC molecule.

20. The pharmaceutical preparation of claim 15, wherein the NA Group 1 molecule is SEQ ID NO:23.

21. The pharmaceutical preparation of claims 15-20, further comprising an adjuvant.

22. The pharmaceutical preparation of claim 15, wherein the agent is a cell expressing an isolated polypeptide comprising the cancer associated antigen or a functional variant thereof, and wherein the cell is nonproliferative.

23. The pharmaceutical preparation of claim 15, wherein the agent is a cell expressing an isolated polypeptide comprising the cancer associated antigen or a functional variant thereof, and wherein the cell expresses a MHC molecule that binds the polypeptide.

24. The pharmaceutical preparation of claim 15, wherein the agent is at least two, at least three, at least four or at least five different polypeptides, each coding for a different cancer associated antigen or functional variant thereof, wherein at least one of the cancer associated antigens is encoded by a NA Group 1 molecule.

25. The pharmaceutical preparation of claim 15, wherein the agent is a PP Group 2 polypeptide.

26. The pharmaceutical preparation of claim 15, wherein the agent is a PP Group 3 polypeptide or a PP Group 4 polypeptide.

27. The pharmaceutical preparation of claim 23, wherein the cell expresses one or both of the polypeptide and the MHC molecule recombinantly.

28. The pharmaceutical preparation of claim 23, wherein the cell is nonproliferative.

29. A composition comprising

an isolated agent that binds selectively a PP Group 1 polypeptide.

30. The composition of claim 29, wherein the PP Group 1 polypeptide is SEQ ID NO:24.

31. The composition of matter of claim 26, wherein the agent binds selectively a PP Group 2 polypeptide.

32. The composition of matter of claim 29, wherein the agent binds selectively a PP Group 3 polypeptide.

33. The composition of matter of claim 29, wherein the agent binds selectively a PP Group 4 polypeptide.

34. The composition of matter of claim 29, wherein the agent binds selectively a PP Group 5 polypeptide.

35. The composition of claims 29-34, wherein the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides.

~~36. The composition of claims 29-34, wherein the agent is an antibody.~~ Cancelled.

~~37. The composition of claim 35, wherein the agent is an antibody.~~

~~38. A composition of matter comprising~~
~~a conjugate of the agent of claims 29-34 and a therapeutic or diagnostic agent.~~ Cancelled

~~39. A composition of matter comprising~~
a conjugate of the agent of claim 35 and a therapeutic or diagnostic agent.

~~40. The composition of matter of claim 38, wherein the conjugate is of the agent and a therapeutic or diagnostic that is a toxin.~~

41. A pharmaceutical composition comprising an isolated nucleic acid molecule selected from the group consisting of NA Group 1 molecules and NA Group 2 molecules, and a pharmaceutically acceptable carrier.

42. The pharmaceutical composition of claim 41, wherein the NA Group 1 molecule is SEQ ID NO:23.

43. The pharmaceutical composition of claim 41, wherein the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule.

44. The pharmaceutical composition of claim 41, wherein the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different cancer associated antigen.

45. The pharmaceutical composition of claims 41-44 further comprising an expression vector with a promoter operably linked to the isolated nucleic acid molecule.

46. The pharmaceutical composition of claims 41-44 further comprising a host cell recombinantly expressing the isolated nucleic acid molecule.

47. ~~A pharmaceutical composition comprising~~
an isolated polypeptide comprising a ~~PP Group 1~~ or a PP Group 2 polypeptide, and a pharmaceutically acceptable carrier.

48. The pharmaceutical composition of claim 47, wherein the PP Group 1 polypeptide is SEQ ID NO:24.

49. The pharmaceutical composition of claim 47, wherein the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.

50. The pharmaceutical composition of claim 47, wherein the isolated polypeptide comprises at least two different polypeptides, each comprising a different cancer associated antigen.

51. The pharmaceutical composition of claim 47, wherein the isolated polypeptides are PP Group 3 polypeptides or MHC binding fragments thereof.

52. The pharmaceutical composition of claim 47, wherein the isolated polypeptides are PP Group 5 polypeptides or MHC binding fragments thereof.

~~53. The pharmaceutical composition of claims 47-52, further comprising an adjuvant.~~

54. An isolated nucleic acid molecule comprising a NA Group 3 molecule.

~~55. An isolated nucleic acid molecule comprising a NA Group 4 molecule.~~

56. An isolated nucleic acid molecule selected from the group consisting of

(a) a fragment of a nucleic acid molecule having a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs. 9, 13, 15, 17, 19, and 23, of sufficient length to represent a sequence unique within the mouse or human genomes, and identifying a nucleic acid encoding a cancer associated antigen precursor,

(b) complements of (a),

provided that the fragment includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of

(1) sequences having the GenBank accession numbers of Table 8,

(2) complements of (1), and

(3) fragments of (1) and (2).

57. The isolated nucleic acid molecule of claim 56, wherein the sequence of contiguous nucleotides is selected from the group consisting of:

(1) at least two contiguous nucleotides nonidentical to the sequence group,

(2) at least three contiguous nucleotides nonidentical to the sequence group,

(3) at least four contiguous nucleotides nonidentical to the sequence group,

(4) at least five contiguous nucleotides nonidentical to the sequence group,

(5) at least six contiguous nucleotides nonidentical to the sequence group,

(6) at least seven contiguous nucleotides nonidentical to the sequence group.

58. The isolated nucleic acid molecule of claim 56, wherein the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

59. The isolated nucleic acid molecule of claim 50, wherein the molecule encodes a polypeptide which, or a fragment of which, binds a MHC receptor or an antibody.

60. An expression vector comprising an isolated nucleic acid molecule of any of claims 54-59 operably linked to a promoter.

61. An expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule.

62. An expression vector comprising a NA Group 1 or Group 2 molecule and a nucleic acid encoding a MHC molecule.

63. The expression vector of claim 62, wherein the NA Group 1 molecule is SEQ ID NO:23.

64. A host cell transformed or transfected with an expression vector of claim 60.

65. A host cell transformed or transfected with an expression vector of any of claims 61-63.

66. A host cell transformed or transfected with an expression vector of claim 60 and further comprising a nucleic acid encoding a MHC molecule.

67. A host cell transformed or transfected with an expression vector of claim 61 and further comprising a nucleic acid encoding a MHC molecule.

68. An isolated polypeptide encoded by the isolated nucleic acid molecule of claim 54 or claim 55.

69. A fragment of the polypeptide of claim 68 which is immunogenic.

70. The fragment of claim 69, wherein the fragment, or a portion of the fragment, binds a MHC molecule or an antibody.

71. An isolated fragment of a cancer associated antigen precursor which, or portion of which, binds a MHC molecule or an antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule.

72. The isolated fragment of claim 71, wherein the NA Group 1 molecule is SEQ ID NO:23.

73. The fragment of claim 71, wherein the fragment is part of a complex with a MHC molecule.

74. The fragment of claim 73, wherein the fragment is between 8 and 12 amino acids in length.

75. An isolated polypeptide comprising a fragment of the polypeptide of claim 68 of sufficient length to represent a sequence unique within the mouse or human genomes and identifying a polypeptide that is a cancer associated antigen precursor.

76. A kit for detecting the presence of the expression of a cancer associated antigen precursor comprising

a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of the NA Group 1 molecules and (b) complements of (a), wherein the contiguous segments are nonoverlapping.

77. The kit of claim 76, wherein the NA Group 1 molecule is SEQ ID NO:23.

78. The kit of claim 76, wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule.

79. A method for treating a subject with a disorder characterized by expression of a cancer associated antigen precursor, comprising

administering to the subject an amount of an agent, which enriches selectively in the subject the presence of complexes of a MHC molecule and a cancer associated antigen, effective to ameliorate the disorder, wherein the cancer associated antigen is a fragment of a cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of

(a) a nucleic acid molecule comprising NA Group 1 molecules,

(b) a nucleic acid molecule comprising NA Group 3 molecules,

(c) a nucleic acid molecule comprising NA Group 5 molecules.

80. The method of claim 79, wherein the NA Group 1 molecule is SEQ ID NO:23.

81. The method of claim 79, wherein the disorder is characterized by expression of a plurality of cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of a MHC molecule and a different cancer associated antigen, wherein at least one of the cancer associated antigens is encoded by a NA Group 1 molecule.

82. The method of claim 81, wherein the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

83. The method of claims 79-82, wherein the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4 and PP Group 5.

84. The method of claims 79-82, wherein the disorder is cancer.

~~85. The method of claims 83, wherein the disorder is cancer.~~

86. A method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject, comprising:

(i) removing an immunoreactive cell containing sample from the subject,

(ii) contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a cancer associated antigen which is a fragment of the precursor,

(iii) introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from the group of nucleic acid molecules consisting of NA Group 1 molecules, NA Group 2 molecules, NA Group 3 molecules, NA Group 4 molecules, and NA Group 5 molecules.

87. The method of claim 86, wherein the NA Group 1 molecule is SEQ ID NO:23.

88. The method of claim 86, wherein the host cell recombinantly expresses a MHC molecule which binds the cancer associated antigen.

89. The method of claim 86, wherein the host cell endogenously expresses a MHC molecule which binds the cancer associated antigen.

90. A method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject, comprising:

(i) identifying a nucleic acid molecule expressed by the cells associated with said condition, wherein said nucleic acid molecule is a NA Group 1 molecule;

(ii) transfecting a host cell with a nucleic acid selected from the group consisting of (a) the nucleic acid molecule identified, (b) a fragment of the nucleic acid identified which includes a segment coding for a cancer associated antigen, (c) deletions, substitutions or additions to (a) or (b), and (d) degenerates of (a), (b), or (c);

(iii) culturing said transfected host cells to express the transfected nucleic acid molecule, and;

(iv) introducing an amount of said host cells or an extract thereof to the subject effective to increase an immune response against the cells of the subject associated with the condition.

91. The method of claim 90, wherein the NA Group 1 molecule is SEQ ID NO:23.

92. The method of claim 90, further comprising identifying a MHC molecule which presents a portion of an expression product of the nucleic acid molecule, wherein the host cell expresses the same MHC molecule as identified and wherein the host cell presents a MHC binding portion of the expression product of the nucleic acid molecule.

93. The method of claim 90, wherein the immune response comprises a B-cell response or a T-cell response.

94. The method of claim 93, wherein the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the cancer associated antigen.

95. The method of claim 90, wherein the nucleic acid molecule is a NA Group 3 molecule.

96. The method of any of claims 90-92, further comprising treating the host cells to render them non-proliferative.

97. A method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising

administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.

~~98. The method of claim 97, wherein the NA Group 1 molecule is SEQ ID NO:23.~~

99. The method of claim 97, wherein the antibody is a monoclonal antibody.

100. The method of claim 99, wherein the monoclonal antibody is a chimeric antibody or a humanized antibody.

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101. A method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject a pharmaceutical composition of any one of claims 13-25 and 37-47 in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject.

102. The method of claim 101, wherein the condition is cancer.

103. The method of claim 101, further comprising first identifying that the subject expresses in a tissue abnormal amounts of the protein.

104. The method of claim 102, further comprising first identifying that the subject expresses in a tissue abnormal amounts of the protein.

105. A method for treating a subject having a condition characterized by expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

(i) identifying cells from the subject which express abnormal amounts of the protein;

(ii) isolating a sample of the cells;

(iii) cultivating the cells, and

(iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

106. The method of claim 105, wherein the NA Group 1 molecule is SEQ ID NO:23.

107. The method of claim 105, further comprising rendering the cells non-proliferative, prior to introducing them to the subject.

108. A method for treating a pathological cell condition characterized by aberrant expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

109. The method of claim 108, wherein the NA Group 1 molecule is SEQ ID NO:23.

110. The method of claim 108, wherein the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

111. The method of claim 108, wherein the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein.

112. The method of claim 108, wherein the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

113. A composition of matter useful in stimulating an immune response to a plurality of a proteins encoded by nucleic acid molecules that are NA Group 1 molecules, comprising

a plurality of peptides derived from the amino acid sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.

114. The composition of matter of claim 113, wherein the NA Group 1 molecule is SEQ ID NO:23.

115. The composition of matter of claim 113, wherein at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto.

116. The composition of matter of claim 115, further comprising an adjuvant.

117. The composition of matter of claim 116, wherein said adjuvant is a saponin, GM-CSF, or an interleukin.

118. The composition of matter of claim 113, further comprising at least one peptide useful in stimulating an immune response to at least one protein which is not encoded by nucleic acid molecules that are NA Group 1 molecules, wherein the at least one peptide binds to one or more MHC molecules.

119. An isolated antibody which selectively binds to a complex of:

(i) a peptide derived from a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule and

(ii) and an MHC molecule to which binds the peptide to form the complex,

wherein the isolated antibody does not bind to (i) or (ii) alone.

120. The isolated antibody of claim 119, wherein the NA Group 1 molecule is SEQ ID NO:23.

121. The antibody of claim 119, wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, or a fragment thereof.

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